Garvey leads extraordinary team effort to win AHA grant to address the intergenerational effects of reproduction on metabolic health and obesity

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The UAB Strategically Focused Obesity Center (SFOC) has been awarded a $3.7 million grant over the next four years from the American Heart Association (AHA), the result of an exceptional collaborative endeavor led by W. Timothy Garvey, MD (third from left in back row), Principal Investigator of the UAB SFOC, Professor and Chair in the UAB Department of Nutrition Sciences, and Director of the UAB Diabetes Research Center (DRC). The group of researchers, some early career scientists serving in leadership roles within the SFOC, worked together to gain funding to pursue a multidisciplinary approach to ascertaining how the in utero environment of mothers with obesity, metabolic syndrome, and gestational diabetes impacts body weight and metabolism of offspring into adulthood, and perpetuates obesity and cardiometabolic disease from one generation to the next. The SFOC team will join investigators studying other aspects of obesity at Johns Hopkins University, New York University Medical Center, and Vanderbilt University, which comprise the AHA’s Strategically Focused Obesity Research Network.

The funded study “Intergenerational Transmission of Obesity” will address the underlying molecular and genetic causes of metabolic abnormalities imprinted in the womb that promote excess weight gain. By assessing mouse models of in utero stress as well as human mothers, newborns, and children over time, the researchers will examine the ability of hormones to influence the regulation of appetite in lean and overweight mothers by affecting such factors as the satisfaction of hunger, the degree of energy expended while the body is at rest, the proficiency by which the body oxidizes fat to generate fuel, and the capability of insulin to control glucose levels. Additionally, they will identify modifications in DNA produced by the environment of the womb—in terms of both mother-to-fetus effect and fetus-to-mother effect—which can have a profound and enduring effect past birth and even change gene expression.

Study participants, chosen prior to or after conception, will be followed through and beyond birth of their offspring. Objective data regarding adiposity, health, and behavior will be obtained through detailed physiologic and behavioral measurements, rather than through less-reliable self-reported
measures. Genotypic information on mothers and offspring, as well as on fathers when possible, will be provided for new hypothesis testing regarding effects in common.

The long-term significance of this research on patient suffering and social costs due to obesity—as well as to diabetes, heart disease, and stroke, of which obesity is a leading contributor—lies in working to break the cycle of obesity being transmitted from generation to generation. “By identifying the very genes, biochemical pathways, and metabolic functions altered in the womb to promote weight gain, we will identify novel targets for intervention to break the cycle of intergenerational obesity,” says Garvey.

David B. Allison, PhD [6] (third from right in back row), Director of the UAB Nutrition Obesity Research Center (NORC) [7] and head of a training component of the SFOC for post-doctoral fellows, says that “the SFOC is uniquely designed to combine expertise in human physiology, maternal-fetal health, epidemiology, molecular biology, and epigenomics to understand the mechanisms causing high rates of obesity.”

Additional team members engaged in both basic and clinical research within the SFOC include Lorie Harper, MD [8], Associate Professor in the Department of Obstetrics and Gynecology [9]; Paula Chandler-Laney, PhD [10], Assistant Professor in the Department of Nutrition Sciences; Cora Elizabeth Lewis, MD [11], Professor in the Division of Preventive Medicine [12]; Kirk Habegger, PhD [13], Assistant Professor in the Division of Endocrinology, Diabetes, and Metabolism [14]; Stella Aslibekyan, PhD [15], Assistant Professor in the Department of Epidemiology [16]; Nengjun Yi, PhD [17], Professor in the Department of Biostatistics [18]; Bertha Hidalgo, PhD [19], Assistant Professor in the Department of Epidemiology; and Nefertiti Durant, MD [20], Associate Professor in the Department of Pediatrics [21].

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